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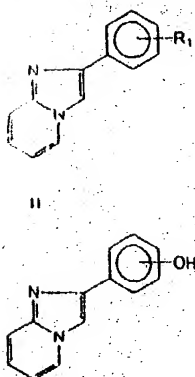
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INDIAN PATENT SPECIFICATION

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(21) Application No. : 104 DEL 92		(71) Applicant : COUNCIL OF SCIENTIFIC AND INDUSTRIAL RESEARCH, Rafi Marg, New Delhi-110001, India, an Indian registered body incorporated under the Registration of Societies Act (Act XXI of 1860).
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Claims : 4		
Text : Pages : Orgs. Sheets. 6 1		Examiner : HARDEV KARAR

(54) Title : A PROCESS FOR THE SYNTHESIS OF NOVEL 2-SUBSTITUTED IMIDAZO (1,2-a)PYRIDINES.

(57) Abstract: A novel 2,3-disubstituted imidazo(1,2-a)pyridines having the formula II where R₁ represents bromo phenyl R₂ represents dialkylaminomethyl, such as diethylaminomethyl, cyclic amino-methyl, like N-morpholinomethyl, N-piperidinomethyl; R₃=R₄=hydrogen is synthesised by reacting a compound of formula I where R₁ represents bromo phenyl R₃ and R₄ represent hydrogen, with formaldehyde and an appropriate secondary amine such as diethylamine, morpholine and piperidine in the presence of an organic solvent such as methanol, ethanol propanol under reflux for 6-12 hr.



EX 3-4

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The invention related to a process for the ^{synthesis} preparation of novel 2-substituted imidazo[1,2-a]pyridines of the formula II shown in the drawing accompanying this specification where R represents substitution;
1

the substituents being ethoxy (3'-OC H), 4'-dialkyla-
2 5

mino-ethoxy such as dimethylamino- ethoxy [4'-
OCH CH N(CH) , cyclic amino ethoxy such as, pyrrolidi-
2 2 3 2

noethoxy (4'-OCH CH NC H) groups.
2 2 4 8

The compounds of the formula II prepared by the process of invention are found to be useful as antiimplantation/abortifacient agents when tested in hamsters for antifertility activity and showed 30-100% protection against pregnancy at 2.5-20 mg/kg by oral and subcutaneous routes.

Accordingly this invention provides a process for the synthesis of novel 2-substituted-imidazo[1,2-a]pyridines having the formula II shown in the drawing accompanying the specification where R represents
1

alkoxy substituents, on phenyl ring; like ethoxy (3'-
OC H), dialkylaminoethoxy such as dimethylaminoet-
2 5

hoxyl[4'-OCH CH N(CH) , cyclic amino ethoxy like pyrol-
2 2 3 2

idinoethoxy(4'-OCH CH NC H) which comprises reacting a
2 2 4 8

phenolic compound of formula I where OH on phenyl ring is at m or p- position(3'-, or 4'-OH) with alkyl halides in presence of organic solvent, like acetone and potassium carbonate at reflux temperature recovering 2-

substituted-imidazo[1,2-a]pyridines by conventional methods.

In a preferred embodiment of the invention, alkyl halides employed may be selected from ethyl bromide, $[C_2H_5Br]$, dimethylaminoethyl chloride $(CH_3)_2NCH_2CH_2Cl$, pyrrolidinoethyl chloride $(C_4H_8N)CH_2CH_2Cl$.

In another preferred embodiment of the invention the solvents used are selected from acetone, DMF and the like.

The compound of the formula I, where hydroxy in phenyl ring is at m or p-position (3'-, or 4'-OH), used as starting material in the process of the invention can be prepared by the process described in our co-pending application No. 102/DEL/92.

The invention is described by the following examples which are given by way of illustration and, therefore, should not be construed to limit the scope of the invention.

EXAMPLE 1

2-[4'-(Pyrolidino)ethoxyphenyl]-imidazo[1,2-a]pyridine of formula (II), where R represent 4'-(pyrolidinoethoxy) group: .

A mixture of 2-(4'-hydroxyphenyl)imidazo[1,2-a]pyridine (420 mg; 2 mmol) N-2-chloroethyl pyrrolidine hydrochloride (408 mg; 2 mmol) and potassium carbonate (4.14 g; 30 mmol) in dry acetone (50 l) was refluxed for 24 hr. The reaction mixture was filtered, the

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inorganic material washed with acetone and the combined filtrate concentrated to obtain a residue which was crystallised from benzene-hexane. The title compound 300 mg, m.p. 109-10^o was obtained in 50% yield.

EXAMPLE 2

2-[4'-(Dimethylamino)ethoxyphenyl]-imidazo[1,2-a]pyridine of formula II, where R represents 4'-(2-dimethyl-₁amino ethoxy) group:

A mixture of 2-(4'-hydroxyphenyl)imidazo[1,2-a]pyridine (420 mg; 2 mmol), 2-dimethylaminoethyl chloride hydrochloride (412 mg 2.4 mmol) and potassium carbonate (4.14 g; 30 mmol) in dry acetone (50 ml) was refluxed for 24 hr. The reaction mixture was filtered and the filtrate concentrated to obtain a residue which was crystallised from Benzene/Hexane to title compound, 337 mg. m.p. 108-9^o in 60% yield.

EXAMPLE 3

2-[3'-Ethoxyphenyl]-imidazo[1,2-a]pyridine Hydrobromide of formula (II) where R represent 3'-ethoxy group₁

A mixture of 2-(3'-hydroxyphenyl)imidazo[1,2-a]pyridine (420 mg, 2 mmol), ethyl bromide (0.23 ml, 3 mmol), and potassium carbonate (4.14 ml 30 mmol) in dry acetone (50 ml) was refluxed for 24 hr. An additional amount of ethyl bromide (1 mmol 0.74 ml) was added after 12 hr. The reaction mixture was filtered, concentrated and purified by silica gel column chromatography. The pure material on treatment with ethanolic

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solution of HBr gave the title compound, 250 mg, m.p. 161-63 ° in 40% yield.

EXAMPLE 4

2-(3'-Ethoxyphenyl)imidazo[1,2-a]pyridine hydrobromide
of formula (II) where R represents 3'-ethoxy group:
1

A mixture of 2-(3'-hydroxyphenyl)imidazo [1,2-a]pyridine (420 mg, 2 mmol), ethyl bromide (0.23 ml 3 mmol) and potassium carbonate (2.07 g, 15 mmol) in dry DMF (10 ml) was stirred at 50 ° for 12 hrs. An additional amount of ethyl bromide (1 mmol) 0.74 ml was added and stirring continued for another 12 hrs. Reaction mixture was filtered, and the filtrate was diluted with water (60 ml) & extracted with chloroform. This, on concentration, gave an oil, which was purified by silica gel column chromatography. The pure material on treatment with ethanolic solution of HBr gave the title compound 317 mg, m.p. 161-63 ° in 50% yield.

We Claim

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1. A process for the synthesis of novel 2-substituted-imidazo[1,2-a]pyridines having the formula II shown in the drawing accompanying the specification where R₁

represents alkoxy substituents, on phenyl ring; like ethoxy(³-OCH₃), dialkylaminoethoxy such as dimethyla-

minoethoxy(⁴'-OCH₂CH₂N(CH₃)₂), cyclic amino ethoxy like

pyrolidinoethoxy(⁴'-OCH₂CH₂NC₄H₈) which comprises

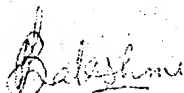
reacting a phenolic compound of formula I where OH on phenyl ring is at m or p- position(³'-, or ⁴'-OH) with alkyl halides in presence of organic solvent, like acetone and potassium carbonate at reflux temperature recovering 2-substituted-imidazo [1,2-a]pyridines by conventional methods.

2. A process as claimed in claim 1, where alkyl halides used in the process is selected from ethyl bromide, 2-dimethylaminoethyl chloride .

3. A process as claimed in claims 1 and 2 where organic solvents used is selected from acetone, DMF .

4. A process for the synthesis of 2-substituted imidazo[1,2-a]pyridines substantially as herein described with reference to the examples.

Dated the 10th day of Feb. 1992.



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Scientist

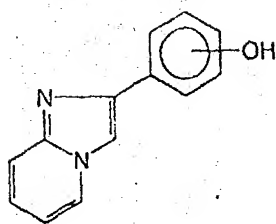
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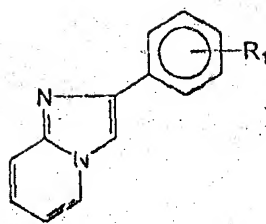
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No. of Sheets 1
Sheet No.

APPL No. 104/DEL/92



I



II

Bakshi
(APPLICANTS)